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Presenting Symptoms: Muscle Tightening and Spasms

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Appropriate Audience: Residents and practicing physicians

Learning Objectives: After completing this educational activity, participant will be able to (1) Differentiate patients with muscle spasms, (2) Establish a comprehensive differential diagnosis for patients with muscle spasms, and (3) Identify differences in history and on electrodiagnostic studies in order to establish a diagnosis.

History

A 22-year-old woman with a 4-year history of insulin dependent diabetes mellitus and hypothyroidism presents to the electrodiagnostic laboratory with a chief complaint of involuntary muscle tightening and spasms. She has not experienced pain in association with the spasms, and she has no muscle cramps. She denies weakness. Her symptoms began 8 years ago while she was in high school, and the muscle tightening and spasms have been slowly progressive in severity and duration. The episodic tightening or twitching of her muscles involves her abdominal, hand, and lower limb muscles bilaterally. These paroxysmal episodes last for approximately 5 seconds and occur many times during the day. On occasion, she notices that objects fall from her hands. She believes that cold may induce her symptoms. Initially, she was not concerned about the abdominal spasms since they helped maintain her muscle tone.

- *Prior to continuing, please develop a differential diagnosis and list each possible diagnosis in order of likelihood.*
- *Is there any additional information regarding the clinical history that might be helpful in clarifying your differential list or changing its order of priority?*

Initial differential diagnosis:

1. Myotonic Dystrophy/Congenital Myotonia
2. Stiff Person Syndrome
3. Isaacs' Syndrome
4. Benign Fasciculations
5. Myopathy
6. Motor Neuron Disease
7. Alcohol Ingestion/Toxic exposure
8. Tremor or dystonia
9. Encephalomyelitis
10. Hypocalcemia/Hypomagnesaemia
11. Hysteria/Malingering

Commentary I

Based on the initial history, a number of causes involving all levels of the nervous system could account for this woman's symptoms. The history of objects falling from her hands and symptoms being exacerbated by cold are reminiscent of complaints associated with



myotonic dystrophy or congenital myotonia. Family history for early onset cataracts, frontal balding, diabetes, neuromuscular disorders, and cognitive impairment is helpful in establishing a diagnosis in this autosomal dominant disorder. Myotonia should only occur with voluntary contraction of muscle. Stiff person syndrome involves the abdominal muscles and is frequently associated with diabetes mellitus. Individuals with stiff person syndrome tend to have a marked startle response and the spasms disappear in sleep. Isaac's syndrome (neuromyotonia), characterized by cramps, fasciculations, pseudomyotonia, and myokymia, is another consideration, although the lack of muscle cramps is highly unusual for this disorder. Furthermore, neuromyotonia is a failure to relax following muscle contraction, and contractions persist during sleep. Benign fasciculations are a diagnosis of exclusion. The lack of muscle cramps or weakness makes a diagnosis of myopathy unlikely, and a 7-year history of muscle twitching without associated weakness would be highly unusual for motor neuron disease. A primary movement disorder, including some form of tremor or dystonia, should be considered, although involvement of the abdominal muscles is highly atypical for either of these problems. Encephalomyelitis is occasionally associated with rigidity. The history of progression would lean against the possibility of a toxic etiology. Alcohol ingestion should be excluded by the history, assuming its accuracy. A 7-year history of hypocalcemia or hypomagnesaemia not associated with tetany and other abnormalities would be unusual.

History, continued

There was no previous history of any other neurological problems. She was the product of a normal pregnancy and birth, and she had appropriate developmental milestones. She was an excellent athlete in school. She denies any cramping, dark coloured urine, weakness, muscle atrophy, bowel or bladder dysfunction, viral illnesses, tremor, unexplained falls, musculoskeletal pain, or toxic exposures. Her husband reports that he has never noticed his wife's muscles twitching while she is sleeping.

There is no family history of early onset diabetes, cataracts, frontal balding, or neurological disorders. She is a social drinker and denies illicit drug use. She has one daughter aged 2 who is healthy. Medications: Synthroid and insulin. Review of systems is unremarkable.

- *If necessary, revise your differential diagnosis based on the additional clinical history.*
- *On which details of the physical examination should you focus at this point?*

Commentary II

There is little support for a clinical diagnosis of myotonic dystrophy, however a congenital myotonia cannot be excluded. Stiff person syndrome, Isaac's syndrome, or even the possibility of malingering should still be considered. Involvement of the abdominal muscles and resolution of symptoms with sleep would lean towards a diagnosis of stiff person syndrome or malingering.

Physical Examination

The patient was in no apparent distress. Examination of the neck, lung, heart, abdomen, and limbs was unremarkable. Neurologic exam: General: alert and oriented with a fluent speech and normal comprehension. Cranial nerves: 2-12 including visual fields and fundoscopic exam were normal. Motor: normal bulk and tone. Power was 5 throughout. There was no percussion myotonia of the tongue or thenar eminence. There was occasional



involuntary twitching of her biceps brachii, triceps, and abdominal muscles. Athetoid movement of the toes was noted. She was able to do repetitive squats without difficulty. Sensory: normal to light touch, pin prick and vibration. There was no sensory level. Reflexes were 2+ throughout and the plantar response produced flexion of the toes. Coordination: finger to nose and heel to shin testing was normal. Rapid alternating movements are unremarkable. Gait including tandem is normal. Romberg is negative.

- *At this point, review your differential diagnosis and revise as appropriate.*
- *Are there additional observations on physical examination that might be helpful in narrowing your differential list?*

Commentary III

Physical examination is essentially unremarkable except for the observed muscle twitching in the abdominal, triceps and bicep brachii muscles as well as some athetoid movements of the toes. There are no physical findings to support an encephalomyelitis, myopathic process, or disorder of motor neurons. Myotonia, while not demonstrated on clinical examination, remains in the differential diagnosis, although it is somewhat less likely. Stiff person syndrome is generally provoked by loud noises, changes in emotion, and startle. In the later stages of stiff person syndrome, contraction of the hip and knee extensor and ankle dorsiflexor muscles develops, as does hyperlordosis of the of the lumbosacral spine secondary to paraspinal muscle contraction. This produces hunching of the shoulders secondary to cervical paraspinal muscle hypertrophy. In Isaac's syndrome, individuals tend to have a stiff posture with slight trunk flexion, shoulder elevation and abduction and elbow flexion. A webbed neck appearance is sometimes created by contraction of the trapezius muscles. Fasciculations and myokymia are particularly prominent in the facial, pectoral, and calf muscles following strong muscle contractions. Delayed relaxation following eye closure or hand closure is characteristic of neuromyotonia (pseudomyotonia).

Physical Examination, continued

There was no startle response, nor did emotion seem to alter her muscle tightening or spasms. There also were no musculoskeletal or postural abnormalities. Sustained closure of the eyes and handgrip did not produce a delay in relaxation.

Previous evaluations included a normal MRI of the brain and cervical spine, as well as normal serum calcium, magnesium, general chemistry, and CK results. A prior EMG was reported as normal. Genetic testing for myotonic dystrophy was normal.

- *If necessary, revise your differential diagnosis based on the additional physical findings.*
- *Design your approach to the electrophysiologic examination based on the existing data.*

Commentary IV

Normal neuroimaging of the brain rules out the possibility of a structural cause for her problem. Serologies are essentially normal and rule out hypocalcemia and hypomagnesemia, as well as a myopathic process. Myotonic dystrophy is ruled out based on genetic testing. Congenital myotonia remains in the differential diagnosis and myotonic discharges should be sought on electrodiagnostic testing, including needle examination on a cooled limb muscle. Electrodiagnostic findings in Isaac's syndrome include the presence of sustained or repetitive spontaneous muscle fiber activity characterized by high frequency



(e.g., 200 to 300 Hz) discharges. Stiff person syndrome is characterized by normal nerve conduction studies. Needle examination is typically normal and the evaluation of a muscle during a spasm reveals continuous motor unit activity associated with normal motor unit action potentials.

Electrophysiologic Data

SENSORY NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
sural sensory calf	L	calf	lateral malleolus	14	39	4.0	45.2
ulnar sensory	L	wrist	proximal and distal phalanx	14	52.6	3.3	53.8

MOTOR NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
peroneal motor ankle	L	ankle	EDB	9	3.9	4.5	-
peroneal motor knee	L	knee	EDB	29.4	3.8	11.1	44.5
ulnar motor wrist	L	wrist	hypothenar	7	13.5	2.8	-
ulnar motor below elbow	L	elbow	hypothenar	19.8	13.5	6.3	56.6

NEEDLE ELECTROMYOGRAPHY									
INSERTional activity: N, sust, unsust FIB: 0, 1+, 2+, 3+, 4+ OTHER: 0 or fascic, myotonia, myokymia EFFort: N, decr RECRuitment: N, inc or dec 1+, 2+, 3+, 4+ AMPLitude: N, inc or dec 1+, 2+, 3+, 4+ DURation: N, inc or dec 1+, 2+, 3+, 4+ POLyphasia: N, inc or dec 1+, 2+, 3+, 4+									
R/L	MUSCLE	INSER	FIB	OTH	EFF	REC	AMP	DUR	POL
L	FDI (hand) [1]	N	0	0	N	N	N	N	N
L	biceps brachii [2]	N	0	0	N	N	N	N	N
L	triceps	N	0	0	N	N	N	N	N
L	deltoid	N	0	0	N	N	N	N	N
L	paraspinal – low cervical	N	0	0	N	N	N	N	N



[1] Hand also cooled to 27.5 degrees centigrade. Needle examination normal.

[2] Brief episode of continuous motor unit activity with normal looking motor unit action potentials observed during muscle twitching.

- *On the basis of both the clinical and electrophysiologic evaluations, formulate your diagnostic impression. List the most likely diagnosis first and follow in order with the other possibilities that are not excluded by the data. Eliminate those diagnoses not supported by the data.*
- *Are there additional electrophysiologic data that you feel would further delineate the diagnosis? (Remember, collecting data that are not needed for the diagnosis is costly and uncomfortable for the patient.)*

Electrophysiologic Data, continued

Nerve conduction studies are normal, as is the needle examination. The normal needle examination eliminates congenital myotonias as well as Isaac's syndrome as possible etiologies for this woman's complaints. No fasciculation potentials were noted on this study, excluding the diagnosis of benign fasciculations. There were no motor unit action potential abnormalities to support a diagnosis of motor neuron disease. The sole finding on the electrodiagnostic study is the presence of continuous, involuntary motor unit activity seen during an episode of twitching of her left biceps brachii. Other than the persistent activity, motor unit recruitment and configuration were normal.

- *Make the final revisions of your diagnostic impression(s).*

Diagnostic Impression

The presence of continuous motor unit activity associated with this individual's clinical history of muscles twitching involving predominantly the abdominal muscles and her history of insulin dependent diabetes mellitus is suggestive of stiff person syndrome.

- *What other diagnostic procedures (laboratory tests, etc.), if any, are needed?*
- *What treatment would you recommend?*

Commentary V

Onset of stiff person syndrome is generally in the fourth or fifth decades and may be serologically confirmed by obtaining anti glutamic acid decarboxylase antibodies (Anti-GAD). A number of individuals are antibody negative but clinically have progressive weakness associated with electrodiagnostic evidence of continuous motor unit activity in the agonist and antagonist muscles. In this individual, the titer was markedly elevated at 112 nmol/L compared to a normal range of 0-0.02 nmol/L. Approximately 33% of individuals with stiff person syndrome have insulin dependent diabetes, and 50% of individuals are noted to have positive oligoclonal bands in their cerebral spinal fluid. Glutamic acid decarboxylase is the rate-limiting step in the production of GABA (an inhibitory neurotransmitter). The presence of anti-GAD antibodies in stiff person syndrome is thought to alter the discharge of the alpha motor neuron and subsequently lead to progressive stiffness.

Stiff person syndrome is characterized by slowly progressive increasing stiffness affecting the axial musculature, predominantly the paraspinal and abdominal muscles as well as the lower and upper limbs. On rare occasion symptoms may be confined to a limb or an upper or lower extremity. Over time there is an increasing frequency in the rate of muscle spasms.



Some attacks of muscle spasms are so severe that individual may be thrown to the floor. Attacks may be triggered by alterations in emotion, startle, and loud noises. Severe cases may have marked contraction of the hip and knee extensors, ankle dorsiflexors, and abdominal and paraspinal muscles. In advanced cases contraction of the paraspinal, abdominal and intercostals muscles may be seen. Hyperlordosis of the lumbosacral spine is common secondary to lumbosacral paraspinal muscles contraction, as is hunching of the shoulders secondary to cervical paraspinal hypertrophy.

Diagnostic criteria for stiff person syndrome include: (1) insidious onset of symptoms with progression, (2) decreased muscle activity with sleep, (3) axial muscular contraction, (4) startle response, (5) decrease muscle activity with diazepam, and (6) continuous motor unit activity on needle examination.

Stiff person syndrome has also been identified as a paraneoplastic syndrome, predominantly in individuals with breast cancer and positive anti-amphiphysin antibodies. A malignancy workup is therefore suggested in individuals with stiff person syndrome. Stiff person syndrome has also been associated with insulin dependent diabetes, Hashimoto's thyroiditis, pernicious anemia, hypoparathyroidism, adrenal failure, myasthenia gravis, vitiligo, and ovarian disease. Cases of stiff person syndrome have also been reported with progressive encephalomyelitis. Variations of stiff person syndrome include: Encephalomyelitis with rigidity syndrome and stiff man syndrome with superimposed myoclonus (Jerking Stiff Man Syndrome).

Muscle spasms are best treated with diazepam 5-10 mg TID-QID. Lioresal 60-90 mg per day and Valproate up to 2 grams per day are alternative therapies for poor diazepam responders. Several small case series have reported success with the use of plasmapheresis or intravenous immunoglobulin.

In this patient, initiation of Diazepam, 10 mg TID produced an 80% reduction in muscle twitching.

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